PB88-161625

Health and Environmental Effects Profile for Benefin

(U.S.) Environmental Protection Agency
Cincinnati, OH

Jan 84

U.S. Department of Commerce
National Technical Information Service
NTIS

PB88-161625

EPA/600/X-84/207
January 1984

HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR BENEFIN

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
OFFICE OF HEALTH AND ENVIRONMENTAL ASSESSMENT
OFFICE OF RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
CINCINNATI, OH 45268

REPRODUCED BY
U.S. DEPARTMENT OF COMMERCE
NATIONAL TECHNICAL
INFORMATION SERVICE
SPRINGFIELD, VA. 22161

TECHNICAL REPORT DATA
(Please read Instructions on the reverse before completing)

1. REPORT NO. EPA/600/X-84/207	2.
3. RECIPIENT'S ACCESSION NO. PB88 161625/AS	
4. TITLE AND SUBTITLE Health and Environmental Effects Profile for Benefin	5. REPORT DATE January 1984
	6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S)	8. PERFORMING ORGANIZATION REPORT NO.
9. PERFORMING ORGANIZATION NAME AND ADDRESS Same as box 12.	10. PROGRAM ELEMENT NO.
	11. CONTRACT/GRANT NO.
12. SPONSORING AGENCY NAME AND ADDRESS Environmental Criteria and Assessment Office Office of Research and Development U.S. Environmental Protection Agency Cincinnati, OH 45268	13. TYPE OF REPORT AND PERIOD COVERED
	14. SPONSORING AGENCY CODE EPA/600/22
15. SUPPLEMENTARY NOTES	

16. ABSTRACT

The Health and Environmental Effects Profile for benefin was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Benefin has been determined to be a systemic toxicant. An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for benefin is 2.5×10^{-1} (mg/kg bw/day) for oral exposure.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field Group

18. DISTRIBUTION STATEMENT Public	19. SECURITY CLASS (This Report) Unclassified	21. NO. OF PAGES 38
	20. SECURITY CLASS (This page) Unclassified	22. PRICE

EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE

DISCLAIMER

This document has been reviewed in accordance with U.S. Environmental Protection Agency policy and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched."

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA docket.

ACKNOWLEDGEMENTS

The initial draft of this report was prepared by Syracuse Research Corporation under Contract No. 68-03-3228 for U.S. EPA's Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH. Dr. Christopher DeRosa was the Technical Project Monitor and Helen Ball was the Project Officer. The final documents in this series were prepared for the Office of Solid Waste, Washington, DC.

Scientists from the following U.S. EPA offices provided review comments for this document series:

Environmental Criteria and Assessment Office, Cincinnati, OH
Carcinogen Assessment Group
Exposure Assessment Group
Reproductive Effects Assessment Group

Editorial review for the document series was provided by:
Judith Olsen and Erma Durden
Environmental Criteria and Assessment Office, Cincinnati, OH

Technical support services for this document series were provided by:
Bette Zwayer, Pat Daunt, Karen Mann, and Jacky Bohanon
Environmental Criteria and Assessment Office, Cincinnati, OH.

TABLE OF CONTENTS

		Page
1.	INTRODUCTION	1
1.1.	STRUCTURE AND CAS NUMBER	1
1.2.	PHYSICAL AND CHEMICAL PROPERTIES	1
1.3.	PRODUCTION DATA	2
1.4.	USE DATA	2
2.	ENVIRONMENTAL FATE AND TRANSPORT PROCESSES	4
2.1.	WATER	4
2.2.	AIR	5
2.3.	SOIL	5
3.	EXPOSURE	11
3.1.	WATER	11
3.2.	FOOD	11
3.3.	INHALATION	11
3.4.	DERMAL	11
4.	PHARMACOKINETICS	12
4.1.	ABSORPTION	12
4.2.	DISTRIBUTION	12
4.3.	METABOLISM	12
4.4.	EXCRETION	13
5.	EFFECTS	14
5.1.	CARCINOGENICITY	14
5.2.	MUTAGENICITY	14
5.3.	TERATOGENICITY	14
5.4.	OTHER REPRODUCTIVE EFFECTS	16
5.5.	CHRONIC AND SUBCHRONIC TOXICITY	16
5.6.	OTHER RELEVANT INFORMATION	16
6.	AQUATIC TOXICITY	17
7.	EXISTING GUIDELINES AND STANDARDS	19
7.1.	HUMAN	19
7.2.	AQUATIC	19
8.	RISK ASSESSMENT	20
9.	REFERENCES	22
APPENDIX:	LITERATURE SEARCHED	29

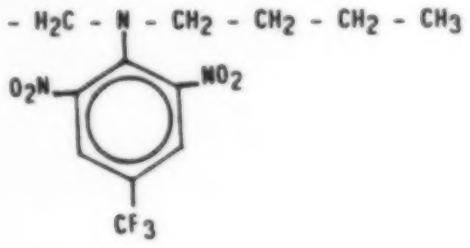
LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
BCF	Bioconcentration factor
GC	Gas chromatography
LC_{50}	Concentration lethal to 50% of recipients
LD_{50}	Dose lethal to 50% of recipients
MAO	Monoamine oxidase
NOEL	No-observed-effect level
ppm	Parts per million
TLC	Thin-layer chromatography
UV	Ultraviolet

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Benefin is the common name for N-butyl-N-ethyl-2,6-dinitro-4-trifluoromethylaniline. It is also commonly referred to as benfluralin. Current Chemical Abstract usage is N-butyl-N-ethyl-2,6-dinitro-4-(trifluoromethyl) benzenamine and was formerly N-butyl-N-ethyl-alpha,alpha,alpha-trifluoro-2,6-dinitro-p-toluidine. Benefin was introduced in 1965 by Eli Lilly and Company under the code number "EL-110" and the trade marks "Balan," "Bonalan" and "Quilan" (BCPC, 1977). Other trade names include Balfin, Banafin, Benalan, Benefex, Benephin, Bethrodine, Binnell, Blulan, Carpidor, Emblem and L54521. The structural and molecular formulae for benefin are as follows:



Molecular formula: $C_{13}H_{16}F_3N_3O_4$

Molecular weight: 335.3

The Chemical Abstract Service (CAS) Registry number is 1861-40-1.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Benefin is a yellow-orange crystalline solid with no appreciable odor (WSSA, 1979). Selected physical properties are listed below.

Melting point:	65-66.5°C	(WSSA, 1979)
Boiling point:	121-122°C at 0.5 mm Hg 148-149°C at 7 mm Hg	(WSSA, 1979)

Vapor pressure:	3.89×10^{-5} mm Hg at 30°C	(WSSA, 1979)
	4×10^{-7} mm Hg at 25°C	(Spencer, 1968)
Solubility at 25°C:		(WSSA, 1979)
Solvent:		
Acetone	65 g/100 mℓ	
Ethanol	2.4 g/100 mℓ	
Xylene	42 g/100 mℓ	
Water	$<1 \times 10^{-4}$ g/100 mℓ	
Water	<1 ppm	(Kenaga, 1980)
Soil adsorption coefficient, K_{OC}:		(Kenaga, 1980)
	experimental	10,700
	predicted	>4,400
BCF:		(Kenaga, 1980)
	calculated from water solubility	>620
	calculated from K_{OC}	850

Benefin is readily soluble in most organic solvents, but has lower solubility in ethanol. It is stable but susceptible to decomposition by UV light (BCPC, 1977).

1.3. PRODUCTION DATA

Benefin is made by nitrating 1-chloro-4-trifluoromethylbenzene with fuming nitric acid and sulfuric acid and then reacting the resultant 1-chloro-2,6-dinitro-4-trifluoromethylbenzene with butylethylamine (WSSA, 1979; BCPC, 1977).

The only domestic producer of benefin is Eli Lilly and Company in Lafayette, IN (SRI, 1983; USITC, 1983). Current production figures are not available; however, consumption figures (Section 1.4.) would indicate that production is on the order of 1 million pounds annually.

1.4. USE DATA

Benefin is used as a preemergence herbicide for control of annual grasses and broad-leaved weeds in crop fields for peanuts, lettuce, tobacco,

lucerne and other forage crops (BCPC, 1977; WSSA, 1979). It should be incorporated into the soil within 4-8 hours after surface application. Usual rates of application for benefin are 1.12-1.5 lb/acre or 1.0-1.35 kg/ha.

In 1976, use of benefin by American farmers was as follows (Eichers et al., 1978): corn, 7000 pounds; soybeans, 10,000 pounds; tobacco, 78,000 pounds; peanuts, 777,000 pounds; alfalfa, <500 pounds; and hay and other forage, 8000 pounds. In 1982, 1.0 million pounds of benefin were used in American peanut fields (U.S. Dept. of Agriculture, 1983). In 1975, it was estimated that domestic benefin use totaled 1.3 million pounds, with 1.1 million pounds in peanuts, 0.1 million pounds in other field crops and 0.1 million pounds in lawns and turf (SRI, 1976).

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

2.1. WATER

The environmental fate or transport of benefin in water has received very little investigation in the available literature. As with other chemicals, the fate of benefin in water will depend on its ability to undergo chemical, photochemical and biological reactions. Hydrolysis data for benefin are not available (see Appendix).

As noted in Section 2.3., photodegradation of benefin from soil surfaces has been shown to occur. However, the rates of photodegradation or its products have not been determined. Therefore, while the photodecomposition of benefin in aquatic media can be predicted to occur, its environmental significance is uncertain without further study. Similarly, benefin decomposition via microbial degradation in soil has been shown to occur, but its environmental significance in aquatic media is uncertain without further study.

The transport of benefin from water via volatilization has not been studied; however, its volatilization from soil surfaces has (see Section 2.3.). It has been noted that an increase in soil moisture content increases the rate of volatilization. Therefore, it is possible that the volatilization transport of benefin is a significant mechanism by which it is lost from the aquatic environment.

Benefin can be strongly adsorbed on soils (see Section 2.3.). Therefore, sorption onto suspended particulate matter in water may possibly occur, followed by partial sedimentation. This possible sorption mechanism of transport has not been investigated.

Kenaga (1980) has predicted BCFs for benefin, based upon water solubility and soil adsorption coefficient (K_{oc}), to be >620 and 850, respectively. Compounds having a BCF in excess of 1000 have a strong potential to

bioaccumulate, while a BCF of <100 indicates that they are not likely to bioaccumulate. The predicted factors for benefin would suggest that this herbicide may be bioconcentrated to a limited degree; however, experimental data are needed to determine the actual degree of bioconcentration, and these data were not found in the literature cited in the Appendix.

The persistence of benefin in water has not been studied and cannot be predicted from available data.

2.2. AIR

Data specific to the fate and transport of benefin in the atmosphere were not found in the literature cited in the Appendix. As noted in Section 2.3., photodegradation of benefin from soil surfaces has been shown to occur. However, the rates of photodegradation or its products have not been determined. Therefore, while photodecomposition of benefin in the atmosphere may occur, its environmental significance is uncertain without further study.

2.3. SOIL

The fate and transport of benefin in soil have been more extensively studied than its fate and transport in air or water. Microorganisms are believed to be a significant mechanism in the disappearance of benefin from soils, although no specific soil organism has been identified as responsible for the degradation (WSSA, 1979). Only one study that indicates the microbial degradation of benefin is available (Golab et al., 1970). This study reports that benefin was 99.9% degraded after 12 hours incubation in artificial rumen fluid utilizing anaerobic conditions. The major identified degradation products were benefin with either one or both nitro groups reduced and benefin with both nitro groups reduced and both alkyl groups removed. In addition, the degradation of benefin in soil under defined anaerobic and aerobic laboratory conditions was studied. Under anaerobic

conditions, 95.4% of the originally incorporated benefin was degraded after 16 days, with the same major degradation products as in the rumen fluid study. Under aerobic conditions, degradation was much slower, with only 50% of the original benefin being degraded after 120 days and 12.1% still remaining after 352 days. A portion of the initial loss of benefin under aerobic conditions was attributed to volatilization. Kaufman and Blake (1973) found no degradation of benefin by Fusarium oxysporum.

Benefin that remains on the soil surface is subject to photodecomposition (WSSA, 1979). Parochetti and Dec (1978) applied ring-labeled ^{14}C-benefin at 1 ppm to thin-layer plates of Hagerstown clay loam soil and measured the effect of 7 days exposure to direct mid-July sunlight. The calculated photodecomposition loss for benefin under these conditions was 17.1% of the initial sample activity. Kennedy and Talbert (1977) found that the loss of benefin in methanol applied at 1 ppm to a silt loam soil averaged 32% after 24 hours exposure to UV light (~310 nm), compared to a 25% loss of an identical sample in the dark at the same 45°C temperature. Parochetti and Hein (1973) applied benefin to a Lakeland sandy soil at a rate of 1.12 kg/ha and sealed it in petri dishes for exposure to UV light (82% of the energy between 290 nm and 340 nm) for either 24 hours or 72 hours. The loss of benefin in the dishes exposed to the UV light was compared to loss in a control group left in the dark. The exposed benefin was found to degrade at a rate slightly faster than the benefin left in the dark.

Data specific to the chemical hydrolysis of benefin in soil were not found in the literature cited in the Appendix.

The transport of benefin from soil due to volatilization has been studied under laboratory conditions. Kennedy and Talbert (1977) found that

volatilization of benefin increased significantly as moisture content was increased in a silt loam soil under UV light at 30°C. At 1% soil moisture content, 20% of the applied benefin (1 ppm) was lost in 24 hours, while at 14% and 26% soil moisture contents 68% and 90%, respectively, of applied benefin was lost in the same time period. A small part of the benefin loss was apparently due to photodecomposition. Reviewing their results with dinitroaniline type herbicides, Kennedy and Talbert (1977) suggested that under field conditions, herbicides with vapor pressures of $1x10^{-6}$ mm Hg or less would be expected to be relatively nonvolatile, whereas herbicides with vapor pressures of $3.9x10^{-5}$ mm Hg or more generally show intermediate to high volatility. The vapor pressure of benefin is $3.9x10^{-5}$ mm Hg at 30°C (WSSA, 1979). In addition, Kennedy and Talbert (1977) showed that soil incorporation significantly decreases losses of benefin from the soil due to volatilization. Parochetti et al. (1976) studied the volatilization of benefin in 3 hours after application to various soils and differing temperatures in a volatility chamber. In a sandy soil (0.5% organic matter), with a 7-15.3% moisture content, from ~3-24% of applied benefin was volatilized in the 3 hours over a temperature range of 30-50°C. At 30°C, volatilization loss was 2.7% in the sandy soil with a 7% moisture content, and 3.5% in sandy soil with a 15.3% moisture content. Volatilization loss increased greatly as the temperature was increased to 50°C. In Hagerstown clay loam (1.9% organic matter, 50°C, 25.8% moisture), ~26% of applied benefin volatilized in 3 hours, while in Littleton silt loam (5.2% organic matter, 50°C, 25% moisture) ~28% volatilized in 3 hours. The authors found that volatilization was not related to soil organic matter or cation exchange capacity. Parochetti and Hein (1973) found that benefin volatilization increased with increasing temperatures (30, 40, 50°C) and increasing

soil moisture content, as described above for Parochetti et al. (1976). Harvey (1974), Jacques and Harvey (1979a) and Yamasue and Worsham (1980) have studied benefin volatility with bioassays in which vapors from benefin applications have inhibited plant growth of foxtail millet, oats and tobacco, respectively. Utilizing laboratory and field experiments, Simoneaux (1969) observed large losses of benefin by volatilization during incubation of moist soil samples and suggested that volatilization was the most important factor responsible for benefin loss from soil.

The leachability of benefin in soils has been studied by a number of investigators. The mobility of benefin in soil was measured by Helling and Dragun (1981) by means of soil TLC and soil column leaching experiments. They found that benefin is immobile in silty clay loam and in clay loam soils (R_f value of 0.00-0.03). The leachability of benefin is expected to be inversely related to adsorbability. Scott and Phillips (1972) found that benefin is strongly adsorbed to silty clay loam (7.1% organic matter) under laboratory conditions. Jacques and Harvey (1979b) measured the adsorption of benefin in 10 Wisconsin soils (0.8-11.7% soil organic matter) and determined that benefin is strongly adsorbed by most soils. The adsorption by the soils appeared to be more closely related to organic matter content than to other soil chemical or physical properties; it seemed likely that organic matter alone was primarily responsible for the adsorption. In addition, Jacques and Harvey (1979b) measured the diffusion of benefin in a diffusion column with silt loam at 55 and 100% of field capacity and at water saturation, and noted that the benefin moved only 10 mm in 17 days. Anderson et al. (1968) studied the leaching of benefin in soil columns filled with a clay loam (1% organic matter) and found that only minute amounts were leached into the column. Harris (1967) measured the relative movement of 28

herbicides in soil columns of silty clay loam (4.3% organic matter) and sandy loam (3.3% organic matter). In clay loam, benefin had the least movement of the 28 herbicides and was relatively immobile in sandy loam. Miller et al. (1978) applied benefin at two application rates (1.7 and 3.4 kg/ha) to a loam soil (<1% organic matter) for 5 years in cotton fields and measured the residues annually and 1 year after treatment. Residues of benefin were essentially confined to the tilled zone in the soil (0-30 cm depth). One year after treatment, residues of benefin were not detected below the tilled zone. In field experiments with preplant application of benefin to peanut fields, Simoneaux (1969) found no residues of benefin in the soil after peanut harvest or beneath the treated soil layer.

Finally, the persistence of benefin in soils has been studied by a number of authors. Jacques and Harvey (1979) used an oat bioassay to determine the persistence of benefin in a silt loam soil under laboratory, greenhouse and field conditions. In the laboratory, benefin was not lost significantly at a constant 5°C temperature for a duration of 248 days. The authors suggested that temperature was an important factor in determining the persistence. In the greenhouse studies, the effect of moisture content on persistence was examined; in air-dry soil, the concentration of benefin fell from the initial level of 0.75 ppm to 0.50 ppm after 29 days and then remained there after 248 days. In wet soil, the concentration of benefin decreased from the initial 0.75 ppm level to 0.40 ppm in 29 days and to 0.26 ppm in 55 days; it was undetectable after 109 days. Under field conditions in 1974 and 1975, the initial concentration of 0.75-1.0 ppm benefin in the soil decreased to the detection limit of 0.10 ppm in ~100-150 days. Zimdahl and Gwynn (1977) studied the soil degradation of benefin in two soils and at two temperatures in the laboratory. The benefin degraded more rapidly in loam soil than in sandy loam and degraded more rapidly at 30°C than at 15°C.

First-order kinetics adequately described the degradation at 15°C, with the half-lives of benefin in loam and sandy loam being 5.6 and 5.7 months, respectively. At 30°C, the data revealed an initial rapid first-order rate of degradation, followed by a slower first-order process. At 30°C, the half-life in loam soil for the initial 2 months was 1.0 month and the half-life from 2-9 months after initiation was 3.8 months. In a greenhouse study, Stoller and Wax (1977) found the half-life of benefin to be 3.0-4.4 months in silty clay loam and 3.0-3.3 months in silt loam. Hurto et al. (1979) examined the degradation of benefin in a silt loam soil and in thatch under aerobic laboratory conditions. After 16 weeks, only ~15% of the benefin had been degraded in the soil, while ~55% had been degraded in the thatch. Miller et al. (1975, 1978) applied benefin (1.12, 1.7, 2.24 or 3.4 kg/ha) to cotton fields as a preplant herbicide for 5 consecutive years and then measured the benefin residue at harvest time annually and at periods up to 30 months after the stopping of treatment. At harvest time, benefin residues of 0.11 (from 2.24 kg/ha treatment) to 1.00 ppmw (from 3.4 kg/ha treatment) still existed in the upper 15 cm of the soil, and residues of 0.02 (from 2.24 kg/ha treatment) to 0.13 ppmw (from 3.4 kg/ha treatment) still existed 30 months and 1 year, respectively, after treatment. Businelli et al. (1975) found that benefin degraded very slowly during the winter, but that degredation increased as the temperature rose; 324 days after soil incorporation, benefin residues were 11-14% of the applied rate. Burnside et al. (1982) noted that benefin degrades to non-phytotoxic levels by the end of the growing season under normal conditions, when applied as a preplant soil-incorporated herbicide for peanuts in the spring. In these studies, no differentiation has been made between volatilization and degradation. WSSA (1979) has reported that at recommended application rates benefin gives 4-5 months of weed control.

3. EXPOSURE

3.1. WATER

The U.S. EPA STORET Data Base contains no listings or data for benefin. Other monitoring data for benefin in water were not found in the available literature.

3.2. FOOD

Monitoring data for benefin exposure in food were not found in the available literature. Benefin is not significantly absorbed or translocated in crops grown in soils treated with the herbicide (WSSA, 1979).

3.3. INHALATION

Monitoring data for benefin exposure in the air were not found in the available literature.

3.4. DERMAL

Monitoring data for benefin exposure to the skin were not found in the available literature. As noted in Section 2.3., benefin can volatilize from soils, particularly after application and before incorporation. At that time, field workers may be exposed to undetermined levels of benefin in the air.

4. PHARMACOKINETICS

4.1. ABSORPTION

Pertinent data regarding the absorption of benefin were not located in the available literature; however, some information was obtained from metabolism studies. Benefin was administered orally to a lactating goat by incorporation of 1 ppm in the feed. Unlabeled benefin was given for 8 days, followed by ^{14}C-labeled benefin for 1 day, followed by unlabeled benefin for 14 days. Samples of urine, feces and milk collected after administration of ^{14}C-benefin (85% carboxy-labeled and 15% uniformly ring-labeled) revealed nearly complete recovery of the radioactivity in urine (10.8%) and feces (89.1%) within 5 days. No statistically significant amount of radioactivity was recovered in the milk of the treated goat as (Golab et al., 1970). This study indicates that the net absorption of benefin and its metabolites from the gastrointestinal tract is small; absorption may either not occur readily or may be rapid but followed by efficient biliary excretion.

4.2. DISTRIBUTION

No pertinent data concerning the distribution of benefin were located in the the available literature.

4.3. METABOLISM

The metabolic fate of benefin was examined both in lactating goats (see Section 4.1.) and in an artificial rumen (Golab et al., 1970). In the rumen experiment, ^{14}C-benefin adsorbed on cellulose was incubated in a bottle that contained a standard mixture of rumen fluid, saliva and carbon dioxide. Aliquots were withdrawn from this mixture at regular intervals and were subjected to radiochemical, TLC and GC analyses. Results of this experiment indicated that 99% of the benefin was degraded after 12 hours of incubation.

At that time, degradation products consisted of uncharacterized extracted polar products (47%), uncharacterized nonextractable products (27%), and various triamines and diamines (25%). It was suggested that the primary degradation product, N-butyl-N-ethyl-alpha,alpha,alpha-trifluoro-5-nitro-toluene-3,4-diamine, gives rise to the polar products, which are ultimately degraded to carbon dioxide and water. In the goat experiment, the ^{14}C-labeled products of benefin in the urine and feces were not characterized. The investigators postulated, however, that the degradation of benefin in the goat system is similar to that in the artificial rumen.

4.4. EXCRETION

The available pertinent information with regard to benefin excretion can be found in Section 4.1.

5. EFFECTS

5.1. CARCINOGENICITY

Pertinent data regarding the carcinogenicity of benefin were not located in the available literature. However, this compound has been nominated to the National Cancer Institute as a candidate for testing. The suspicion that benefin may be carcinogenic was based on its structural similarity to trifluralin, a known carcinogen. Because of this similarity, and because of its commerical importance as a preemergence herbicide on peanuts, benefin was recommended for testing (Helmes et al., 1982).

5.2. MUTAGENICITY

Benefin failed to exhibit mutagenicity in a variety of microbial assays. Summarized in Table 5-1, these included: 1) reverse mutation tests on numerous histidine-requiring strains of Salmonella typhimurium (Shirasu, 1975; Shirasu et al., 1976; Andersen et al., 1972; Moriya et al., 1983) and on two strains of tryptophane-dependent Escherichia coli (Shirasu, 1975; Shirasu et al., 1976; Moriya et al., 1983); and 2) a rec-assay on two strains of Bacillus subtilis. Inclusion of the S-9 activating system in some of the reverse mutation assays involving Salmonella typhimurium and Escherichia coli made no difference with regard to mutagenic response (Moriya et al., 1983).

On the other hand, Bulgarian scientists reported that benefin produced chromosome aberrations and inhibited mitotic spindle formation in the roots of Vicia faba (Ruseva, 1978). However, no experimental details regarding dose or technique were given.

5.3. TERATOGENICITY

Pertinent data regarding the teratogenicity of benefin were not located in the available literature.

TABLE 5-1

Mutagenicity Testing of Benefin

Assay	Species	Strain	Concentration/ Dose	Application Method	Activation System (S-9)	Response	Reference
Rec-assay	Bacillius subtilis	H17 rec+ and rec-	20 µg/plate	spot test	-	-	Shirasu et al., 1976; Shirasu, 1975
Reverse mutation	Escherichia coli	B/r WP2 hcr+	20 µg/plate	spot test	-	-	
		B/r WP2 hcr-	20 µg/plate				
Reverse mutation	Escherichia coli	WP2 hcr	0-5000 µg/plate	plate incorporation	+/-	-	Moriya et al., 1983
Reverse mutation	Salmonella typhimurium	TA1535 his	20 µg/plate	spot test	-	-	Shirasu, 1975; Shirasu et al., 1976
		TA1536 his	20 µg/plate		-	-	
		TA1537 his	20 µg/plate		-	-	
		TA1538 his	20 µg/plate		-	-	
Reverse mutation	Salmonella typhimurium	8 his-requiring strains (nonspecified)	1-5 µg/plate	plate incorporation	-	-	Andersen et al., 1972
Reverse mutation	Salmonella typhimurium	TA100	0-5000 µg/plate	plate incorporation	+/-	-	Moriya et al., 1983
		TA98	0-5000 µg/plate		+/-	-	
		TA1537	0-5000 µg/plate		+/-	-	Moriya et al., 1983
		TA1538	0-5000 µg/plate		+/-	-	

5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding other reproductive effects of benefin were not located in the available literature.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

Three-month feeding tests involving benefin yielded "no-effect levels" of 1250 ppm for rats and >500 ppm for dogs (BCPC, 1977). Information regarding experimental details and the criteria by which the no-effect levels were determined was not given.

5.6. OTHER RELEVANT INFORMATION

LD_{50} values (mg/kg bw) for an acute oral dose of benefin were reported as >10,000 for rats, >5000 for mice and >2000 for rabbits, dogs and chickens (BCPC, 1977). Hungarian scientists reported an inflammatory effect of benefin when it was applied to the upper eyelids of rats (Molnar and Molnar, 1976). The technique employed entailed monitoring the detention of Evans Blue in the eyelid; however, no other details were given. In addition, Bulgarian scientists reported that benefin inhibited MAO activity in the brains and livers of rats. Animals were given a 1/10 LD_{50} oral dose of benefin daily for 6 days. Livers and brains were subsequently extracted, homogenized and assayed for MAO with kynuramine (Bainova et al., 1980).

6. AQUATIC TOXICITY

The acute lethality of benefin has been determined for three species of freshwater fish (Johnson and Finley, 1980; Tooby et al., 1975) and the freshwater crustacean Gammarus fasciatus (Sanders, 1970). As summarized in Table 6-1, the 96-hour LC_{50} values in fish and the crustacean were near 1.0 mg/ℓ, but in the harlequin fish and the crustacean scud, the commercial product Balan (which may contain 18% benefin) was administered. Based on the 4-day toxicity data in the harlequin fish, Tooby et al. (1975) extrapolated and estimated the 3-month LC_{50} for this species at 1.0 µg/ℓ.

Additional data on the acute or chronic toxic effects of benefin to aquatic animal or plant species were not located in the available literature. Data on the persistence and accumulation of benefin residues in the aquatic environment were also not available.

TABLE 6-1

Acute Lethal Effects of Benefin to Freshwater Aquatic Animals

Species	Duration (hours)	LC_{50} (mg/ℓ)	Method	Reference
Fathead minnow, *Pimephales promelas*	96	0.8	static	Johnson and Finley, 1980
Goldfish, *Carassius auratus*	96	<1.0	static	Johnson and Finley, 1980
Harlequin fish, *Rasbora heteromorpha*	24	1.4[a]	all	Tooby et al., 1975
	48	1.3[a]		
	96	1.2[a]	constant-flow	
Scud, *Gammarus fasciatus*	24	8.2[b]	static	Sanders, 1970
	48	4.0[b]	static	
	96	1.1[b]	static	

[a] Balan containing 18% benefin was administered.

[b] Technical balan was administered.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

Under the Federal Food, Drug and Cosmetic Act, a tolerance of 0.05 ppm has been established for residues of benefin in or on alfalfa, clover, birdsfoot trefoil (Federal Register, 1967a) and lettuce (Federal Register, 1967b).

7.2. AQUATIC

Guidelines and standards for the protection of aquatic species from the toxic effects of benefin were not found in the literature cited in the Appendix.

8. RISK ASSESSMENT

In the four studies cited in Section 5.2., benefin was not found to be mutagenic to Salmonella typhimurium, Escherichia coli, or Bacillus subtilis (Shirasu, 1975; Shirasu et al., 1976; Andersen et al., 1972; Moriya et al., 1983). A Bulgarian study (Ruseva, 1978), however, reported chromosome aberrations and inhibition of mitotic spindle formation when roots of Vicia faba were treated with unspecified doses of benefin. Data regarding the carcinogenicity or teratogenicity of benefin were not found in the available published literature.

A Bulgarian study (Bainova et al., 1980) indicated that oral administration of benefin to rats at a level of 1/10 LD_{50}/day for 6 days caused inhibition of MAO activity in the brain and liver. The authors speculated that behavioral disturbances in workers exposed to pesticides such as benefin might be related to interference with biogenic amine metabolism.

The British Crop Protection Council (BCPC, 1977) reported NOELs for rats and dogs exposed orally to benefin for 3 months. These values were 1250 ppm for rats and >500 ppm for dogs. Since experimental details were not given, a value for an ADI cannot be calculated from these data.

Statements concerning available literature in this document refer to published, quotable sources and are in no way meant to imply that confidential data, which this document could not address, are not in existence. These data, which are considered Confidential Business Information (CBI), are available in summary form as a CBI Appendix that can be accessed by individuals with appropriate clearance. Conclusions from the CBI Appendix regarding risk assessment can, however, be presented in this chapter as follows.

The CBI Appendix to this document reviews other animal data, from which an ADI of 0.25 mg/kg bw/day or 17.5 mg/day for a 70 kg man was derived. The ADI was based on a NOAEL of 25 mg/kg bw/day for effects on the erythron in dogs in a chronic oral study, and an uncertainty factor of 100 (10 to account for species to species extrapolation and 10 for protection of unusually sensitive individuals within the population).

9. REFERENCES

Andersen, K.J., E.G. Leighty and M.T. Takahashi. 1972. Evaluation of herbicides for possible mutagenic properties. J. Agric. Food Chem. 20: 649-656.

Anderson, W.P., A.B. Richards and J.W. Whitworth. 1968. Leaching of trifluralin, benefin and nitralin in soil columns. Weed Sci. 16(2): 165-169.

Bainova, A., Z. Zaprianov and F. Kaloyanova-Simeonova. 1980. Effect of pesticides on the activity of monoamine oxidase (MAO) in rats. Proc. Int. Congr. Occup. Health. 1: 531-535.

BCPC (British Crop Protection Council). 1977. Benfluralin. In: Pesticide Manual, 5th ed., H. Martin and C.R. Worthing, Ed. BCPC Publications, Worcestershire, England. p. 31.

Burnside, K.R., D.A. Addison, R.B. Cooper, R.D. Hicks and H.L. Webster. 1982. Benefin degradation rate and effect on subsequent rotation crops in the southeast. Proc. South. Weed Sci. Soc. 35: 56-63. (CA 97:051129j)

Businelli, M., F. Tafuri, L. Scarponi and C. Marucchini. 1975. Persistence of benflural in soil and its uptake by carrots. Pestic. Sci. 6(5): 475-480. (CA 84:131325s)

Eichers, T.R., P.A. Andrilenas and T.W. Anderson. 1978. Farmers' Use of Pesticides in 1976. U.S. Dept. of Agriculture, Economics, Statistics and Cooperative Service, Washington, DC. Agriculture Economic Report No. 418. p. 37-38.

Federal Register. 1967a. N-butyl-N-ethyl-alpha,alpha,alpha-trifluoro-2,6-dinitro-p-toluidine; tolerances for residues. Fed. Regist. 32: 13807.

Federal Register. 1967b. N-Butyl-N-ethyl-alpha,alpha,alpha-trifluoro-2,6-dinitro-p-toluidine. Tolerances for residues. Fed. Regist. 32: 17472.

Golab, T., R.J. Herberg, J.V. Gramlich, A.P. Raun and G.W. Probst. 1970. Fate of benefin in soils, plants, artificial rumen fluid and the ruminant animal. J. Agr. Food Chem. 18(5): 838-844.

Harris, C.I. 1967. Movement of herbicides in soil. Weeds. 15(3): 214-216.

Harvey, R.G. 1974. Soil adsorption and volatility of dinitroaniline herbicides. Weed Sci. 22(2): 120-124.

Helling, C.S. and J. Dragun. 1981. Soil leaching tests for toxic organic chemicals. In: Test Protocols for Environmental Fate and Movement of Toxicants. Proc. of a Sym. Assoc. of Official Anal. Chem. 94th Annual Meeting, Washington, DC. p. 43-88.

Helmes, C.T., V.A. Fung, B. Lewin, K.E. McCaleb, S. Malko and A.M. Pawlovich. 1982. A study of aromatic nitro compounds for the selection of candidates for carcinogen bioassay. J. Environ. Sci. Health. A17(1): 75-128.

Hurto, K.A., A.J. Turgeon and M.A. Cole. 1979. Degradation of benefin and DCPA in thatch and soil from a Kentucky bluegrass (Poa pratensis) turf. Weed Sci. 27(2): 154-157. (CA 92: 1244y)

Jacques, G.L. and R.G. Harvey. 1979a. Dinitroaniline herbicide phytotoxicity as influenced by soil moisture and herbicide vaporization. Weed Sci. 27(5): 536-539.

Jacques, G.L. and R.G. Harvey. 1979b. Adsorption and diffusion of dinitroaniline herbicides in soils. Weed Sci. 27(4): 450-455.

Jacques, G.L. and R.G. Harvey. 1979c. Persistence of dinitroaniline herbicides in soil. Weed Sci. 27(6): 660-665.

Johnson, W.W. and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Fish and Wildlife Service, Resource Publication 137. U.S. Dept. of the Interior, Washington, DC.

Kaufman, D.D. and J. Blake. 1973. Microbial degradation of several acetamide, acylanilide, carbamate, toluidine and urea pesticides. Soil Biol. Biochem. 5(3): 297-308.

Kenaga, E.E. 1980. Predicted bioconcentration factors and soil sorption coefficients of pesticides and other chemicals. Ecotoxicol. Environ. Safety. 4: 26-38.

Kennedy, J.M. and R.E. Talbert. 1977. Comparative persistence of dinitroaniline type herbicides on the soil surface. Weed Sci. 25(5): 373-381.

Miller, J.H., P.E. Keeley, C.H. Carter and R.J. Thullen. 1975. Soil persistence of trifluralin, benefin and nitralin. Weed Sci. 23(3): 211-214.

Miller, J.H., P.E. Keeley, R.J. Thullen and C.H. Carter. 1978. Persistence and movement of ten herbicides in soil. Weed Sci. 26(1): 20-27.

Molnar, J. and A. Molnar. 1976. Quantitative evaluation of acute inflammatory activity of ocular irritants on the eyelid in rats. Egeszsegtudomany. 20(2): 156-160.

Moriya, M., T. Ohta, K. Watanabe, T. Miyazawa, K. Kato and Y. Shirasu. 1983. Further mutagenicity studies on pesticides in bacterial reversion assay systems. Mutat. Res. 116(3-4): 185-216.

Parochetti, J.V. and E.R. Hein. 1973. Volatility and photodecomposition of trifluralin, benefin and nitralin. Weed Sci. 21(5): 469-473.

Parochetti, J.V. and G.W. Dec, Jr. 1978. Photodecomposition of eleven dinitroaniline herbicides. Weed Sci. 26(2): 153-156.

Parochetti, J.V., G.W. Dec, Jr. and G.W. Burt. 1976. Volatility of eleven dinitroaniline herbicides. Weed Sci. 24(6): 529-532.

Ruseva, E. 1978. Cytological effect of the herbicides Regione, Gramoxone and Balan. Genet. Sel. 11(5): 330-337. (Bul.) (CA 93(13): 126721z)

Sanders, H.O. 1970. Toxicities of some herbicides to six species of fresh water crustaceans. J. Water Pollut. Contr. Fed. 42(8): 1544-1550.

Scott, H.D. and R.E. Phillips. 1972. Diffusion of selected herbicides in soil. Soil Sci. Soc. Am. Proc. 36(5): 714-719.

Shirasu, Y. 1975. Significance of mutagenicity testing on pesticides. Environ. Qual. Saf. 4: 226-231.

Shirasu, Y., M. Moriya, K. Kato, A. Furuhashi and T. Kada. 1976. Mutagenicity screening of pesticides in the microbial system. Mutat. Res. 40: 19-30.

Simoneaux, B.J. 1969. Processes of retention and loss of benefin in soil. Diss. Abstr. Int. B. 30(5): 1986-1987.

Spencer, E.Y. 1968. Guide to the Chemicals Used in Crop Protection, Fifth edition. Publication 1093, Canada Dept. of Agriculture, Research Branch. Ontario, Canada.

SRI (Stanford Research Institute). 1976. Herbicides. In: Chemical Economics Handbook. SRI, Menlo Park, CA. p. 573.7008 G-H.

SRI (Stanford Research Institute) International. 1983. 1983 Directory of Chemical Producers: United States of America. SRI International, Menlo Park, CA. p. 773.

Stoller, E.W. and L.M. Wax. 1977. Persistence and activity of dinitroaniline herbicides in soil. J. Environ. Qual. 6(2): 124-127.

Tooby, T.E., P.A. Hursey and J.S. Alabaster. 1975. Acute toxicity of 102 pesticides and miscellaneous substances to fish. Chem. Ind. (London). 12: 523-526.

U.S. Dept. of Agriculture. 1983. Inputs Outlook and Situation. IOS-2, October. Economic Research Service, Washington, DC. p. 11.

USITC (United States International Trade Commission). 1983. Synthetic Organic Chemicals. U.S. Production and Sales, 1982. USITC Publication 1422. U.S. International Trade Commission. Washington, DC. p. 227.

WSSA (Weed Science Society of America). 1979. Benefin. In: Herbicide Handbook of the Weed Science Society of America, 4th ed. WSSA, Champaign, IL. p. 41-45.

Yamasue, Y. and A. D. Worsham. 1980. Effects of benefin vaporizing from soils on tobacco (Nicotiana tabacum) foliage. Weed Sci. 28(3): 306-311.

Zimdahl, R.L. and S.M. Gwynn. 1977. Soil degradation of three dinitroanilines. Weed Sci. 25(3): 247-251.

APPENDIX:
LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of:

CA SEARCH (Files 308, 309, 310, 311, 320)
TOXLINE
MEDLINE
RTECS
SCI SEARCH
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE

These searches were conducted in November, 1983. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7th), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. Documentation of the Threshold Limit Values, 4th ed. (Includes Supplemental Documentation, 1981, 1982, 1983). Cincinnati, OH. p. 486.

ACGIH (American Conference of Governmental Industrial Hygienists). 1983. TLVs: Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1983-84. Cincinnati, OH. p. 94.

BCPC (British Crop Protection Council). 1977. Pesticide Manual, 5th ed. Martin, H. and C.R. Worthing, Ed. British Crop Protection Council. p. 593.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2A. John Wiley and Sons, NY. p. 2878.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2B. John Wiley and Sons, NY. p. 2879-3816.

Clayton, G.D. and F.E. Clayton, Ed. 1982. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2C. John Wiley and Sons, NY. p. 3817-5112.

Grayson, M. and D. Eckroth, Ed. 1978-83. Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed. John Wiley and Sons, NY. 23 Volumes.

Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology, 3rd ed. Publishing Sciences Group, Inc., MA. p. 575.

ITII (International Technical Information Institute). 1982. Toxic and Hazardous Industrial Chemicals Safety Manual for Handling and Disposal with Toxicity and Hazard Data. ITII, Tokyo, Japan. p. 700.

NTP (National Toxicology Program). 1983. Carcinogenesis Testing Program. Chemicals on Standard Protocol. Management Status.

Ouellette, R.P. and J.A. King. 1977. Chemical Week Pesticide Register. McGraw-Hill Book Co., NY.

Sax, I.N. 1979. Dangerous Properties of Industrial Materials, 5th ed. Van Nostrand Reinhold Co., NY.

SRI (Stanford Research Institute). 1983. Directory of Chemical Producers. Stanford, CA.

U.S. EPA. 1982. Chemical Activities Status Report, 3rd ed. (EPACASR). Offices of Pesticides and Toxic Substances, Washington, DC. EPA 560/TIIS-82-002b.

U.S. EPA. 1983. Status Report on Rebuttable Presumption Against Registration (RPAR) or Special Review Process. Registration Standards and the Data Call In Programs. Office of Pesticide Programs, Washington, DC.

U.S. EPA. 1983. CHIB Existing Chemical Assessment Tracking System. Name and CAS Number Ordered Indexes. Office of Toxic Substances, Washington, DC.

USITC (United States International Trade Commission). 1983. Synthetic Organic Chemicals. U.S. Production and Sales, 1982. Washington, DC. USITC Publication 1422.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY.